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Mihnea-Alexandru Gaman

Carol Davila University of Medicine and Pharmacy, Bucharest, Romania

Elena-Codruta Dobrica

Carol Davila University of Medicine and Pharmacy, Bucharest, Romania

Emilia G. Pascu

Craiova University of Medicine and Pharmacy, Craiova, Romania

Matei-Alexandru Cozma

Carol Davila University of Medicine and Pharmacy, Bucharest, Romania

Mirela-Elena Epingeac

Craiova University of Medicine and Pharmacy, Craiova, Romania

See next page for additional authors

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Authors

Mihnea-Alexandru Gaman, Elena-Codruta Dobrica, Emilia G. Pascu, Matei-Alexandru Cozma, Mirela-Elena Epingeac, Amelia M. Gaman, Anca M. Pantea Stoian, Ovidiu G. Bratu, and Camelia C. Diaconu



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Research article

Cardio metabolic risk factors for atrial fibrillation in type 2 diabetes mellitus: Focus on hypertension, metabolic syndrome and obesity

Mihnea A. Găman^{1*}, Elena C. Dobrică¹, Emilia G. Pascu², Matei A. Cozma¹,
Mirela E. Epîngeac², Amelia M. Găman³, Anca P. Stoian¹, Ovidiu G. Bratu¹,
Camelia C. Diaconu⁴

¹Carol Davila University of Medicine and Pharmacy, Bucharest, Romania

²Craiova University of Medicine and Pharmacy, Craiova, Romania

³Craiova University of Medicine and Pharmacy, Department of Pathophysiology, Filantropia Hospital, Department of Hematology, Craiova, Romania

⁴Carol Davila University of Medicine and Pharmacy, The Clinical Emergency Hospital of Bucharest, Department of Internal Medicine, Bucharest, Romania

Abstract

Objective. Atrial fibrillation (AF) in type 2 diabetes mellitus (T2DM) has been little explored so far. However, there are several cardio metabolic risk factors for AF in T2DM patients, such as arterial hypertension, obesity or the metabolic syndrome. Our objective was to evaluate cardio metabolic risk factors for AF in T2DM patients. **Methods.** We studied the medical records of T2DM patients hospitalized in the Internal Medicine department of an emergency referral hospital in Bucharest, Romania. The study was observational, retrospective and carried out between January-June 2018. **Results.** The study group included 221 T2DM patients (with a mean age of 68.65 ± 10.64 , ranging between 37-93 years): 116 women (52.49%; with a mean age of 70.53 ± 10.69 , ranging between 37-93 years) and 105 men (47.51%; with a mean age of 66.57 ± 10.23 , ranging between 38-91 years). 92 patients had AF (41.63%): 40 women (34.48%) and 52 men (49.52%). 180 patients (81.45%) were hypertensive: 103 women (88.79%) and 77 men (73.33%). 113 patients (51.13%) had metabolic syndrome: 58 women (50.00%) and 55 men (52.38%). 77 patients (34.84%) were obese: 45 women (38.79%) and 32 men (30.48%). AF patients associated obesity in 26 cases (28.26%), hypertension in 73 cases (79.35%) and metabolic syndrome in 56 cases (60.87%). **Conclusions.** Out of the study group, 92 T2DM patients (41.63%) had AF, men being more likely to suffer from AF than women ($p=0.0288$). Hypertension affected 180 patients (81.45%) and in greater proportion women vs. men ($p=0.0051$). The metabolic syndrome and obesity were discovered in 113 patients (51.13%) and 77 patients (34.84%), respectively, with no significant differences in terms of gender. In our research, the highest cardio metabolic risk factors for AF in T2DM were hypertension (OR = 3.6675) and the metabolic syndrome (OR = 3.3388).

Keywords : diabetes mellitus, atrial fibrillation, hypertension, obesity, metabolic syndrome, risk factors.

Highlights ✓ Patients with type 2 diabetes mellitus are at increased risk of developing atrial fibrillation.
✓ Hypertension, metabolic syndrome and obesity are important cardio metabolic risk factors for atrial fibrillation in patients with type 2 diabetes mellitus.

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✉ *Corresponding author: Mihnea-Alexandru Găman, Carol Davila University of Medicine and Pharmacy, Bucharest, Romania;
E-mail: mihneagaman@yahoo.com

Introduction

Out of the cardiac arrhythmias, atrial fibrillation (AF) is undoubtedly the most frequently encountered entity in clinical practice (1). The number of patients with AF has been growing steadily up to the point in which this disorder has become an epidemic: in 2030, more than 12 million people will be affected by AF in the United States (1, 2).

Age, male sex, type 2 diabetes mellitus (T2DM), obesity, hypertension, heart failure and metabolic syndrome are some of the risk factors involved in the development of AF (3-5). The relationship between T2DM and AF is complex and of particular interest. A recent Danish cohort study, conducted on 253.374 T2DM patients vs. 4.827.713 subjects without T2DM, has postulated that, in the development of AF, T2DM is an independent risk factor and that younger subjects with T2DM are at higher risk of AF vs. elderly T2DM subjects (6).

The cardio metabolic risk factors for AF have been intensively studied in the past decade and particular attention has been paid to the metabolic syndrome. Many studies have shown conflicting results regarding the impact of the metabolic syndrome on AF development, with some suggesting that AF is rather linked to some components of the metabolic syndrome rather than to the metabolic syndrome itself (5). The metabolic syndrome, defined as the co-occurrence of several metabolic risk factors in a single patient, can be easily diagnosed in a routine check-up and it is a common finding among Romanian patients, some studies reporting a prevalence >65% (7).

Thus, our objective was to evaluate cardio metabolic risk factors for AF in T2DM patients, particularly focusing on the metabolic syndrome, hypertension and obesity.

Materials and Methods

Study design

A cross-sectional observational retrospective study was conducted to evaluate cardio metabolic risk factors for AF in patients diagnosed with T2DM.

Setting

The study was conducted from January to June 2018 in the Internal Medicine Clinic of a tertiary care teaching center located in Bucharest, Romania.

Participants

A total of 221 patients were included in the study, representing all patients diagnosed with T2DM who were

referred to the Internal Medicine Clinic from January to June 2018.

Data sources and variables

The data were collected by utilizing electronic medical records of patients diagnosed with T2DM. The information obtained from the medical records was collected by means of a structured form that included: age, sex, comorbidities and treatment.

Bias

To reduce selection bias, we included all patients diagnosed with T2DM in the time period of the study. Patients with incomplete medical records were excluded.

Statistical methods

Categorical variables were presented as frequencies and percentages. Continuous variables were presented as the mean \pm SD. Patients were divided according to the presence and absence of AF, metabolic syndrome, obesity and hypertension. Categorical variables were compared using Fisher's exact test.

Continuous variables were compared using independent t-test samples. The level of significance was presented as p-values in different tables. The analysis was performed at a 5% level of significance using Microsoft Excel (Microsoft Office Professional Plus 2013), MedCalc (<https://www.medcalc.org>) and GraphPad QuickCalcs (<https://www.graphpad.com>).

Ethical standards

The study was conducted in accordance with the national law and the Declaration of Helsinki (1975), as revised in 2008 (5). All patients signed an informed consent upon admission, agreeing to have their medical records reviewed for scientific purposes as long as their confidentiality is respected.

Results

The study group included 221 patients diagnosed with T2DM (with a mean age of 68.65 ± 10.64 , ranging between 37-93 years): 116 women (52.49%; with a mean age of 70.53 ± 10.69 , ranging between 37-93 years) and 105 men (47.51%; with a mean age of 66.57 ± 10.23 , ranging between 38-91 years). 92 patients had AF (41.63%): 40 women (34.48%) and 52 men (49.52%). 180 patients (81.45%) were hypertensive: 103 women (88.79%) and 77 men (73.33%). 113 patients (51.13%) had metabolic syndrome: 58 women (50.00%) and 55 men (52.38%). 77 patients (34.84%) were obese: 45 women (38.79%) and 32 men (30.48%). These results are presented in Table 1.

Table 1. The characteristics of patients included in the study

| | Women | | Men | | p-value |
|---------------------|---------------------|--------------|---------------------|-------------|---------|
| Age | 70.53 ± 10.69 years | | 66.57 ± 10.23 years | | 0.0080 |
| Number | 116 (52.49%) | | 105 (47.51%) | | - |
| Atrial fibrillation | Yes | 40 (34.48%) | Yes | 52 (49.52%) | 0.0288 |
| | No | 76 (65.52%) | No | 53 (50.48%) | |
| Hypertension | Yes | 103 (88.79%) | Yes | 77 (73.33%) | 0.0051 |
| | No | 13 (11.21%) | No | 28 (26.67%) | |
| Metabolic syndrome | Yes | 58 (50.00%) | Yes | 55 (52.38%) | 0.7879 |
| | No | 58 (50.00%) | No | 50 (47.62%) | |
| Obesity | Yes | 45 (38.79%) | Yes | 32 (30.48%) | 0.2063 |
| | No | 71 (61.21%) | No | 73 (69.52%) | |

AF patients associated obesity in 26 cases (28.26%), hypertension in 73 cases (79.35%) and the metabolic syndrome in 56 cases (60.87%), as seen in Table 2 (OR = odds ratio, CI = confidence intervals).

Discussions

In the current study, 221 patients with T2DM were recruited over a period of six months based on the medical records of the Internal Medicine Clinic of a referral emergency hospital in Bucharest, Romania. Out of this group, 92 patients (41.63%) had also been diagnosed with AF, men being more likely to suffer from AF than women ($p=0.0288$), as similar studies have previously reported (8, 9). Hypertension affected 180 patients (81.45%), women in a greater proportion than men ($p=0.0051$). The metabolic syndrome and obesity were discovered in 113 (51.13%) and 77 patients (34.84%), respectively, with no significant differences in

terms of gender. In our research, the highest cardio metabolic risk factors for AF in T2DM were hypertension (OR = 3.6675) and the metabolic syndrome (OR = 3.3388).

The management of both type 1 and type 2 diabetes mellitus will still remain a challenge, even in the near future: the prevalence of diabetes in the United States is rapidly growing, with reports estimating that by 2030 more than 54.9 million people will suffer from diagnosed or undiagnosed diabetes, as opposed to approximately 35.6 million people in 2015 (10). As compared to the general population, patients diagnosed with T2DM are more likely to suffer from AF as well: Zethelius et al. investigated which are the risk factors for AF in T2DM and concluded that there was a strong association between obesity/body mass index, hypertension and albuminuria and AF in T2DM (11).

The pathophysiology of AF in T2DM is complex. Hyperglycemia and hypertension are key players in the development of AF in patients with diabetes: hyperglycemia leads to increased levels of inflammatory markers, reactive oxygen species and advanced glycosylation end products at a myocardial level, promoting atrial fibrosis, whereas hypertension promotes atrial dilatation (12). Atrial dilatation is also enhanced by the proliferation of atrial fibroblasts. Both conditions lead to structural and electrical remodeling of the left atrium and explain the development of AF in T2DM (1, 13, 14). The contribution of oxidative stress might also be determined by additional exposure to exogenous sources of ROS, as well as the reduced capacity of antioxidant defense systems to scavenge these molecules in the elderly since their efficiency is age-dependent (15,16).

Irrespective of its relationship with T2DM, AF should be appropriately managed. Therapeutic solutions include either rate control or rhythm control options and, in patients with CHA₂DS₂-VASc score of at least one point, anticoagulation agents should be prescribed to prevent thromboembolism and cardiovascular mortality (1, 17-19).

Table 2. Cardio metabolic risk factors for AF in T2DM

| | AF + | | AF - | | OR | 95% CI | p-value |
|--------------------|------|-------------|------|--------------|--------|-----------|---------|
| Hypertension | Yes | 73 (79.35%) | Yes | 66 (51.16%) | 3.6675 | 1.99-6.76 | <0.0001 |
| | No | 19 (20.65%) | No | 63 (48.84%) | | | |
| Metabolic syndrome | Yes | 56 (60.87%) | Yes | 41 (31.78%) | 3.3388 | 1.91-5.84 | <0.0001 |
| | No | 36 (39.13%) | No | 88 (68.22%) | | | |
| Obesity | Yes | 26 (28.26%) | Yes | 23 (17.83%) | 1.8155 | 0.96-3.44 | 0.0677 |
| | No | 66 (71.74%) | No | 106 (82.17%) | | | |

Conclusions

Cardio metabolic risk factors for AF (hypertension, metabolic syndrome and obesity) were found in a substantial percentage in the study group. Women were more likely to be hypertensive than men. There were no statistically significant differences between genders regarding the metabolic syndrome or obesity. In the study group, 41.63% of the patients diagnosed with T2DM also associated AF. Diabetic men were more likely to have AF than women. AF was strongly associated with hypertension and metabolic syndrome in diabetic patients.

Author contribution

MAG and CCD designed the study. MAG, ECD, MAC, EGP and MEE collected the data. MAG analyzed the data and wrote the paper. AMG, APS and CCD critically revised the paper. The manuscript was read and approved by all authors.

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Conflict of interest disclosure

There are no known conflicts of interest in the publication of this article. The manuscript was read and approved by all authors.

Compliance with ethical standards

Any aspect of the work covered in this manuscript has been conducted with the ethical approval of all relevant bodies and that such approvals are acknowledged within the manuscript.

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